

FIG. 1A

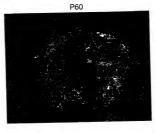
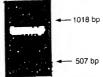


FIG. 1B

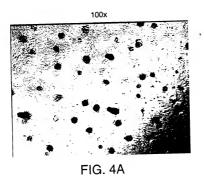


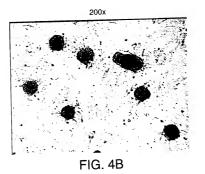
FORWARD PRIMER [GCGGGGCGGTGCGTGACTAC] REVERSE PRIMER [GGGTGGTGAGGGTTGAGGTTTGTG] FIG. 2

NECTIN POSITIVE CELLS PROLIFERATE AROUND ISLETS IN VITRO



FIG. 3





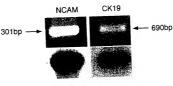


FIG. 5

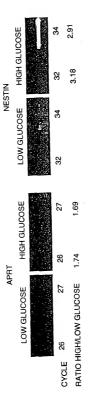


FIG. 6

Nestin Amino Acid Sequence:

"MEGCMGEESFOMWELNRRLEAYLGRVKALEEQNELLSAGLGGLR RQSADTSWRAHADDELAALRALVDQRWREKHAAEVARDNLAEELEGVAGRCEQLRL ARERTTEEVARNRRAVEAEKCARAWLSSQGAELERELEALRVAHEEERVGLNAQAAC APRLPAPPRPPAPAPEVEELARRLGEAWRGAVRGYQERVAHMETSLDQTRERLARAVQ

 ${\tt EVRLELQQLQAERGGLLERRAALEQRLEGRWQERLRATEKFQLAVEALEQEKQGLQSQ}$ IAQVLEGRQQLAHLKMSLSLEVATYRTLLEAENSRLQTPGGGSKTSLSFQDPKLELQF PRTPEGRRLGSLLPVLSPTSLPSPLPATLETPVPAFLKNQEFLQARTPTLASTPIPPT ${\tt PQAPSPAVDAEIRAQDAPLSLLQTQGGRKQAPEPLRAEARVAIPASVLPGPEEPGGQR}$ QEASTGQSPEDHASLAPPLSPDHSSLEAKDGESGGSRVFSICRGEGEGQIWGLVEKET AIEGKVVSSLQQEIWEEEDLNRKEIQDSQVPLEKETLKSLGEEIQESLKTLENQSHET LERENQECPRSLEEDLETLKSLEKENKRAIKGCGGSETSRKRGCRQLKPTGKEDTQTL QSLQKENQELMKSLEGNLETFLFPGTENQELVSSLQENLESLTALEKENQEPLRSPEV GDEEALRPLTKENQEPLRSLEDENKEAFRSLEKENQEPLKTLEEEDQSIVRPLETENH KSLRSLEEQDQETLRTLEKETQQRRRSLGEQDQMTLRPPEKVDLEPLKSLDQEIARPL ENENQEFLKSLKEESVEAVKSLETEILESLKSAGQENLETLKSPETQAPLWTPEEINK ${\tt SGGNESSRKGNSRTTGVCGSEPRDIQTPGRGESGIIEISGSMEPGEFEISRGVDKESO}$ ${\tt RNLEEEENLGKGEYQESLRSLEEEGQELPQSADVQRWEDTVEKDQELAQESPPGMAGV}$ ENKDEAELNLREQDGFTGKEEVVEQGELNATEEVWFPGEGHPENPEPKEQRGLVEGAS VKGGAEGLQDPEGQSQQVGTPGLQAPQGLPEAIEPLVEDDVAPGGDQASPEVMLGSEPAIGNEGARD AND STREET FOR STRAMGESAAGAEPGLGQGVGGLGDPGHLTREEVMEPPLEEESLEAKRVQGLEGPRKDLEEAGGLGTEFSELPGKSRDPWEPPREGREESEAEAPRGAEEAFPAETLGHTGSDAPSPWP LGSEEAEEDVPPVLVSPSPTYTPILEDAPGLQPQAEGSQEASWGVQGRAEAGKVESEQ EELGSGEIPEGLQEEGEESREESEEDELGETLPDSTPLGFYLRSPTSPRWTPLESRGH ${\tt PLKETGKEGWDPAVLASEGLEEPSEKEEGEEGEEECGRDSDLSEEFEDLGTEAPFLPG}$ ${\tt VPGEVAEPLGQVPQLLLDPAAWDRDGESDGFADEEESGEEGEEDQEEGREPGAGRWGP}$ ${\tt GSSVGSLQALSSSQRGEFLESDSVSVSVPWDDSLRGAVAGAPKTALETESQDSAEPSG}$ ${\tt SEEESDPVSLEREDKVPGPLEIPSGMEDAGPGADIIGVNGQGPNLEGKSQHVNGGVMN}$ ${\tt GLEQSEESGARNALVSEGDRGSPFQEEEGSALKRSSAGAPVHLGQGQFLKFTQREGDR}$ FSWSSGED"

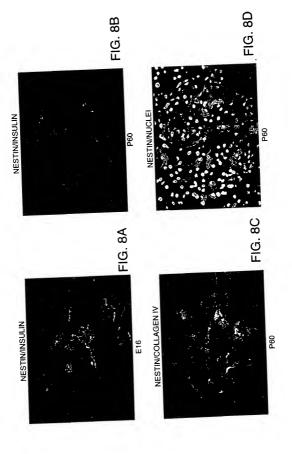
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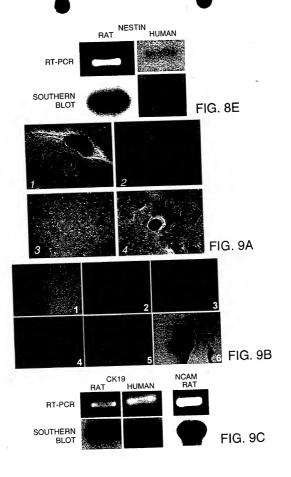
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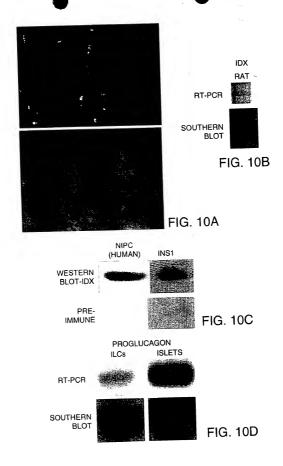
FIG. 7B

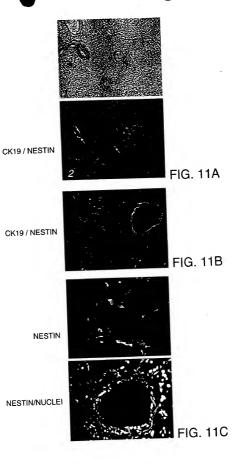
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FIG. 7C









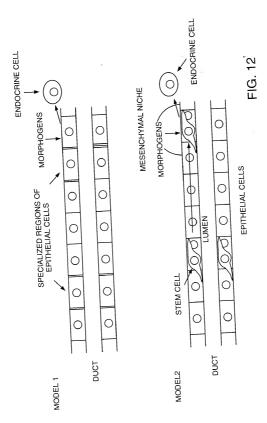




FIG. 13A



FIG. 13B

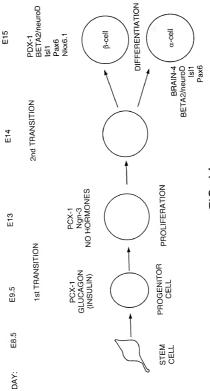
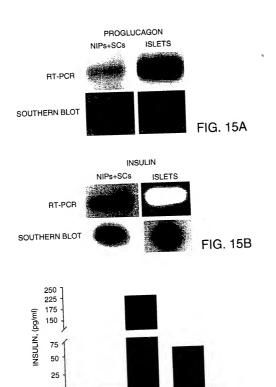


FIG. 14



DISH 1

CONTROL

FIG. 15C

DISH2

TREATMENT

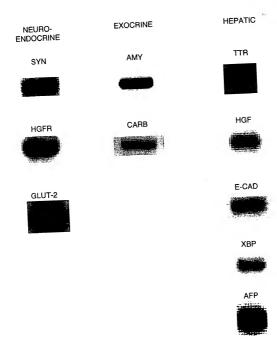


FIG. 16

Figure 17

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SEQ ID NO: 4

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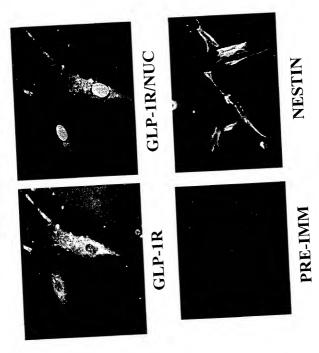


Figure 184





346bp

NIPs

Islets



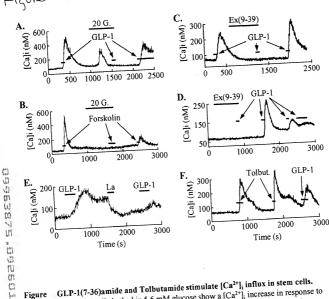
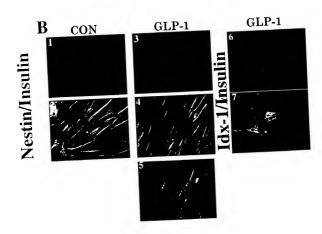


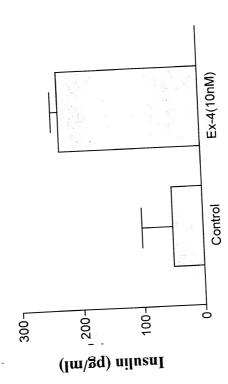
Figure GLP-1(7-36)amide and Tolbutamide stimulate [Ca²⁺], influx in stem cells. (A) Fura 2 loaded cells bathed in 5.6 mM glucose show a [Ca²⁺], increase in response to

10 nM GLP-1. Increasing the extracellular glucose to 20 mM (20 G) also caused an increase of [Ca²⁺], but application of GLP-1 in 20 mM glucose failed to produce a [Ca²⁺], response. A third application of GLP-1 on returning to 5.6 mM glucose produced a [Ca²⁺]; response. (B) The glucose-dependent effects of GLP-1 were reproduced by 10 mM forskolin, suggesting that $[Ca^{2+}]_i$ elevation is cAMP-mediated. (C) The GLP-1 mediated increase of $[Ca^{2+}]_i$ was reversibly inhibited by 10 nM exendin (9-39). This effect is not due to receptor desensitization (D) as application of GLP-1 in the presence of exendin (9-39) failed to produce a response whereas subsequent applications of GLP-1 after washout of exendin produced repeated [Ca²⁺], elevations. (E) The GLP-1-mediated increase of [Ca²⁺], is inhibited by 0.5 mM extracellular La³⁺, suggesting that GLP-1 stimulates Ca²⁺ influx. (F) Stem cells bathed in 5.6 mM glucose were stimulated with 100 µM tolbutamide (Tolbut.) and respond to repeated applications with increases in [Ca²⁺]. Application of 10 nM GLP-1 also stimulates an increase of [Ca²⁺], suggesting that GLP-1 acts by depolarizing the cells.









Transfected with hIDX-1 and







Transfected with hIDX-1 and incubated with Vehicle (PBS)





XAI /uilusuI